

Aetiology of Asymptomatic Raised Serum Alanine Amino-transferase in Patients with Type 2 Diabetes Mellitus

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Abstract

Background: Elevated level of serum alanine aminotransferase (ALT) is not uncommon in routine laboratory test. This study was aimed to find out the aetiology of asymptomatic raised ALT in hospitalized type 2 diabetes mellitus (T2DM) patients.

Methods: This cross-sectional study was done in BIRDEM over a period of six month. T2DM patients having asymptomatic raised serum ALT were evaluated clinically and by laboratory tests.

Results: Total number of patients was 53. Among them male were 39 and female were 14. Male and female ratio was 2.8:1. Mean age was 49.2±7.9 years. Mean body mass index (BMI) was 25.5±5 kg/m². Among the study subjects, 25 (47.2%) were overweight and 16 (30.2%) were obese. Hypertension, hepatomegaly and dyslipidaemia were present in 29 (54.7%), 11 (20.8%) and 36 (67.96%) cases respectively. Non-alcoholic fatty liver disease (NAFLD) was the commonest (37, 69.8%) aetiology for raised ALT in this study. Seropositivity for hepatitis B virus (HBV) surface antigen (HBsAg) and antibody against hepatitis C virus (anti-HCV) were present in 7 and 5 cases respectively. In 4 cases cause could not be identified. Most of the cases with >5 times raised ALT had hepatitis B or C infection.

Conclusion: Elevation of serum ALT is common in T2DM patients. NAFLD is the commonest cause followed by hepatitis B and C virus infection.

Keywords: alanine aminotransferase; asymptomatic; type 2 diabetes mellitus; non-alcoholic fatty liver disease.

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Introduction

Abnormal liver function test results in routine blood examination are a prevalent condition in general population. It is frequently overlooked and often inadequately investigated. It may be an indicator of significant liver disease. Individuals with type 2 diabetes mellitus (T2DM) have a higher incidence of liver function test abnormalities than non diabetics.^{1,2} Mild chronic elevations of transaminases often reflect underlying insulin resistance.² This study was aimed to find out the aetiology of raised alanine amino transferase (ALT) among hospitalized adult type 2 diabetic patients.

Methods

This cross-sectional study was done in Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) from July

to December 2011. Hospitalized adult male and non-pregnant female T2DM patients with raised ALT were evaluated in this study. Patients with acute viral hepatitis, known chronic liver disease, dengue fever and septicemia were excluded. Body mass index (BMI) was calculated as body weight in kilogram divided by height in meters square. ALT was estimated using enzymatic methods. We defined ALT more than 40 U/L as abnormal. Ultrasonography was performed in all cases as well as viral markers and other necessary tests were done to identify the aetiology.

Results

Total number of patients was 53. Among them male were 39 and female were 14. Baseline characteristics are presented in Table I. Most (43, 81.1%) patients had sedentary lifestyle. Among the study subjects, 25 (47.2%) were overweight and 16 (30.2%) were obese. Hypertension, hepatomegaly and dyslipidaemia were present in 29 (54.7%), 11 (20.8%) and 36 (67.9%) cases respectively. Regarding the magnitude of raised ALT, most (41, 77.4%) of study subjects had ALT between 2-5 times of upper normal limit (UNL), (Table II).

Table I. Base-line characteristics of the study population

Characteristics	Results
Mean age (years)	49.2±7.9
Male: Female	2.8:1
Mean BMI (kg/m ²)	25.5±5

Table II. Magnitude of raised ALT among the study population

Magnitude of raised ALT	Frequency (Percentage)
<2 times of UNL*	7 (13.2)
2-5 times of UNL	41 (77.4)
>5 times of UNL	5 (9.4)

*UNL= upper normal limit

Non-alcoholic fatty liver disease (NAFLD) was the commonest aetiology for raised ALT in this study (Table III). Other causes included hepatitis B virus (HBV) and C virus (HCV) infection. In 7.5% cases no cause could be identified. Most of the cases with >5 times raised ALT had hepatitis B or C infection.

Table III. Aetiology of raised ALT among the study population

Aetiology	Frequency (Percentage)
Non-alcoholic fatty liver disease (NAFLD)	37 (69.8)
HBsAg positive	7 (13.2)
Anti-HCV positive	5 (9.4)
Unidentified	4 (7.5)

Discussion

The occurrence of liver disease and raised liver enzymes is common in T2DM and may be multifactorial in origin. The different liver abnormalities in diabetes cover the entire spectrum from asymptomatic transaminitis to cirrhosis.² Liver disease is an important comorbid condition in T2DM subjects. One study published in 2006, done by West et al. showed that elevated ALT was found in 9.5% of T2DM patients.³ Persistent elevation of ALT in asymptomatic patient accounts much of the challenge in clinical practice. In another study, Mohamad Nejad et al. found higher prevalence of elevated ALT and aspartate amino-transferase (AST) in T2DM than general population.⁴

The most common cause of elevated liver enzymes in T2DM patients is NAFLD.⁵ In the United States, NAFLD is replacing alcoholic hepatitis and viral hepatitis as the most common etiology of chronically elevated serum ALT in both diabetic and non-diabetic individuals.¹ In our study, NAFLD had been found among 37 (69.8%) study subjects which was consistent with the findings of other studies.

Several studies described a higher prevalence of NAFLD among people with T2DM compared with non-diabetics, with prevalence estimates ranging from 40% to 69.5%.⁶⁻⁸ Moreover, a recent case-control study demonstrated that people with T2DM had on an average 80% more liver fat than age, weight and sex-matched controls.⁹ This difference was not explained by the type of medications used. Furthermore, AST and ALT underestimated liver fat content among people with diabetes; for any given ALT or AST level, adults with T2DM had 40 to 200% more liver fat than non-diabetic adults.⁹ Patients with T2DM not only have a higher prevalence of NAFLD, but also appear to have more severe forms of the disease, including non-alcoholic steatohepatitis (NASH) and fibrosis.¹⁰⁻¹⁴

HBV infection had been found to be 60% more prevalent among persons with diabetes in United States.¹⁵ In different studies HBV sero-positivity was found 2-4%.^{16,17} HBV infection outbreaks have been reported among diabetic patients who share a blood glucose meter without cleaning and disinfecting between uses, associated with limited awareness of the high risk for HBV transmission during finger stick blood glucose monitoring.¹⁸ In our study, the prevalence of HBsAg positive was 13.2%.

The lower frequency of anti-HCV sero-positivity had been shown in two studies.^{19,20} Several studies, from different countries, had reported that 13–33% of patients with HCV infection had diabetes, mostly T2DM,²¹ compared with the prevalence of 4–10% for non-HCV control population.²² These data suggested that patients with HCV were 3 times more likely to develop DM than individuals who were HCV negative. We found 9.4% of our study subjects were anti-HCV positive. In one study from Bangladesh, Mahub MM et al. found that the commonest etiology of raised serum ALT among newly detected DM and IGT patients was NAFLD followed by hepatitis B and C virus infection.²³

Limitations of the study

Short study period and small sample size were limitations of current study. Fibroscan and liver biopsy could not be done.

Conclusion

NAFLD is the commonest cause of raised ALT among patients with T2DM. Raised levels of ALT should be evaluated, so that potentially treatable cases can be identified and measures might be taken to reduce morbidity and disease transmission in infective cases.

Conflict of interest: None

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